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EXAMINER
MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
1652	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/830,837	Applicant(s) SEIDAH ET AL.	
	Examiner William W. Moore	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-56,59-75 and 80-83* is/are pending in the application.

4a) Of the above claim(s) *50 and 62-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-49,51,52,54,55,59-61,65-75 and 80-83* is/are rejected.

7)☒ Claim(s) *53 and 56* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 & 11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse in Paper No. 15, filed April 1, 2003, of Group 3, including claims 30, 31, 33, 36-46, 65, 67-75 and 80-83 to the extent that they describe a third disclosed product which is a human SKI-1 protease having an amino acid sequence comprising either or both of a catalytic domain from positions 187 through 997 of SEQ ID NO:6 and a propeptide domain from positions 18 through 137 of SEQ ID NO:6, and to a first method of making the product utilizing a polynucleotide encoding same and vectors and host cells comprising the polynucleotide, as well as to a first method of use of the catalytic domain product in cleaving a substrate thereof other than a sterol-regulatory element-binding protein, is acknowledged.

The traversal is on the grounds that search and examination of two or more Groups of inventions would not constitute a "serious burden". This is not found persuasive with respect to the requirement as between the product of Group 3 and products of Groups 1 and 2 because the restriction requirement, Paper No. 14 mailed February 26, 2003, explained why each product was patentably distinct, because Applicant neither alleges nor suggests that any one of the distinct products would be obvious over another or that one product shares a common technical feature which is special with another product, or otherwise identifies such a special technical feature permitting a singular search, and because conducting one or more additional sequence searches constitutes a burden on the resources available for examination.

Applicant's arguments are, however, persuasive with respect to the requirement for restriction as between Group 3 and Groups 4 and 6 insofar as the latter Groups describe a human SKI-1 protease fragment comprising a propeptide domain with an amino acid sequence from position 18 through position 137 of SEQ ID NO:6, or disclosed variant

thereof, capable of binding to a human SKI-1 proprotease having an amino acid sequence from positions 18 through 1052 of SEQ ID NO:6. Because the amendment to claim 66 of Paper No. 15 brings this claim within the invention of Group 3 and because the prior art made of record herewith either anticipates, renders obvious, or excludes, the methods of claims 47-49, peptides of claims 51-56 and methods of claims 59 and 60, Applicant's arguments are persuasive with respect to the requirement for restriction as between Group 3 and Groups 4, 6, 9, and 16. Therefore the restriction requirement as between Groups 3, 4, 6, 9, and 16 is RESCINDED and claims 30-49, 51-56, 59, 60, 65-75, and 80-83 are examined herein to the extent they describe peptides of claim 51, methods of use of these peptides of claims 59 and 60, a SKI-1 protease having an amino acid sequence comprising either or both of a propeptide domain from positions 18 through 137 or a catalytic domain from positions 187 through 996 of SEQ ID NO:6, wherein a propeptide domain, or variant thereof, is capable of binding to a SKI-1 proprotease of SEQ ID NO:1 and forming a tight complex therewith, a method of making this product utilizing a polynucleotide encoding same and vectors and host cells comprising the polynucleotide, as well as to methods of use of the catalytic domain in producing a fragment thereof, cleaving a substrate thereof, or producing protein or peptide precursors from substrates thereof. The requirement for restriction as between the product of Group 3 and products of Groups 1 and 2, as well as between the products and methods of Groups 3, 4, 6, 9, and 16, and products and methods of Groups 5 and 7, 8, 10-15 and 17-20 is still deemed proper and is therefore made FINAL. Claims 30-49, 65-75 and 80-83 are withdrawn in part, and claims 50 and 61-64 are withdrawn entirely, from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

Priority

Receipt is acknowledged of a copy of Applicant's initial priority document, Canadian Patent Application serial No. 2,249,648, filed 04 November 1998, which provides

support for certain disclosures in the International Application No. PCT/CA99/01058 filed 04 November 1999, which constitutes the disclosure of the present U.S. utility application serial No. 09/830,837. Disclosures of the present specification that have a priority date of November 4, 1998 are as follows:

Page 1, line 1, through page 2, line 7;
Page 2, lines 18-28;
Page 9, line 8, through page 12, line 30, and Figures 1-12; and,
Page 16, line 21, through page 26, line 35.

Consequently, the remaining disclosures at page 2, lines 8-16; between page 2, line 29, and page 9, line 5; between page 12, line 31 and page 16, line 19, and Figures 13-30; and present in Examples 2-6 and the RESULTS paragraph at pages 27 through 55 of the specification have a priority date of November 4, 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-45, 47-49, 65-75 and 80-83 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31-35, 45, 47, 49 and 66 are rejected as indefinite because the term, "proteic" that Applicant introduces at line 1 in claims 31-35, 45, and 66, at lines 2 and 4 of claim 47, at line 2 of claim 49, and twice in the terminal clause of claim 66, has no ordinary meaning in the relevant arts or in common English usage. The written description fails to clearly define the term so as to put one reasonably skilled in the art on notice that the applicant intended to define that claim term. The term "proteic" in claims 31-35, 45, 47, 49, and 66 is apparently used by Applicant to mean "related to a protein". In addition to a lack of any meaning in contemporary English or an accepted meaning in the arts of molecular biology and biochemistry, the term is superfluous where Applicant had no need to state "proteic" in claims 36, 46, 59 or 60. Claims 36-44, 48, 65, 67-75

and 80-83 are included in the rejection where they depend from claims 31-35 and 47 but fail to correct or otherwise remedy the ambiguity of claims from which they depend.

Claim Rejections - 35 USC §§ 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

Claims 30-33, 45-49, 51-52, 54, 55, 59, 60, 65-69, 72, and 80-83 are rejected under 35 U.S.C. §102(e) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Brown et al., U.S. Patent No. 6,322,962, made of record herewith

The U.S. Patent to Brown et al.('962) is prior art under 35 U.S.C. §102(e) based on the August 14, 1998, priority date for its disclosure. The amino acid sequence set forth in SEQ ID NO:3 of Brown et al.('962) of a human Site-1 protease is identical to the amino acid sequence of the human SKI-1 protease set forth in SEQ ID NO:6 herein, thus all further reference to amino acid positions will be made to SEQ ID NO:6 herein. The limitation "named SKI-1" in claims 30, 32, and 59-61 provides no patentable distinction where nomenclature is subjective and the amino acid sequence of the Site-1 protease set

forth in SEQ ID NO:3 of Brown et al.('962) is identical to the amino acid sequence of the SKI-1 protease set forth in SEQ ID NO:6 herein. Brown et al.('962) is applied under 35 U.S.C. §102(e) whether the ambiguous claim limitation "proteic fragment" in claims 30, 47, and 66, from which claims 36, 40-46, 48, 49, 65, 72, and 80-83 ultimately depend, remains in the claims or not. In the claims, the term is considered to embrace a soluble, enzymatically active, SKI-1fragment comprising an amino acid sequence from position 187 through position 996 of SEQ ID NO:6 and further comprising one or more amino acids of the amino acid sequence of SEQ ID NO:6 that flank either or both of positions 187 and 996 of SEQ ID NO:6 because such larger fragments would be "proteic". Brown et al.('962) remains anticipatory prior art to the claimed subject matter if no meaning were given to the term "proteic" and the claim construed as though it were absent because claim 30 also embraces, see line 3, a non-specific "variant" of a fragment comprising an amino acid sequence from position 187 through position 996 of SEQ ID NO:6 that may further comprise one or more amino acids within the sequence of SEQ ID NO:6 flanking either or both of positions 187 and 996 of SEQ ID NO:6. Because Brown et al.('962) discuss hamster and human SKI-1 amino acid sequences interchangeably, see, e.g., cols. 5-6, and because the amino acid sequences are 98% identical, one to another, the further disclosures of Brown et al.('962) relating to manipulations of, expression of, proteolytic activity of, and substrate recognition of, the hamster SKI-1 protease are considered to inherently anticipate manipulations of, expression of, proteolytic activity of, and substrate recognition of, the human SKI-1 protease.

It is noted that if the term "proteic" and the phrase, "a variant thereof", were both removed from claim 30, Brown et al.('962) would be considered to have rendered the claimed subject matter obvious to one of ordinary skill in the art at the time the invention was made. This is because Brown et al.('962) teach that proteolytically active SKI-1

fragments will have a naturally-occurring amino terminus at position 187 of SEQ ID NO:6 and that a soluble proteolytically active SKI-1 fragment may have a carboxyl-terminus within the range of positions between 995 and 1000 of SEQ ID NO:6.

Brown et al.('962) disclose, cols. 5-6 and Figure 4, the preparation of soluble forms of a human Site-1/SKI-1 protease which may have an amino acid sequence identical to SEQ ID NO:6 herein comprising a deletion of the transmembrane region beyond an amino acid position at "about 995", including positions "at about 1000" in order to provide a substantially less lipophilic version of the protease that retains proteolytic activity, said deletion in the protease amino acid sequence resulting from deletion of the nucleic acid sequence encoding the SKI-1 protease having the amino acids sequence set forth in SEQ ID NO:6. Brown et al.('962) further disclose, col. 16, lines 29-44, and Figures 11A and 11B, that cellular proteolysis of a portion of the prodomain of the SKI-1 that results in an amino terminus at position 187 permits its transport to the Golgi apparatus, well-known in the art as a portal to the secretory pathway in mammalian cells. Brown et al.('962) also disclose, cols. 16-17 and 62-64, the preparation of a variant polynucleotide encoding a truncated SKI-1 protease variant lacking the transmembrane region and transfection of a Chinese hamster ovary [CHO] cells with the variant polynucleotide to express, and then isolate, a soluble, truncated SKI-1 variant lacking a transmembrane region and having an amino terminus at position 187 of SEQ ID NO:6, thus anticipating claims 30, 45, 46, 65 and 66 where the cleavage produces a "fragment" – less than the whole – which is an SKI-1 enzyme and a variant of a fragment having a carboxyl-terminus at position 996 yet lacking a transmembrane region. The fragment is released into the medium of the CHO cells thus Brown et al.('962) disclose a composition of claim 65. Because the SKI-1 protease prodomain cleaved in producing the truncated SKI-1 variant lacking that has an amino terminus at position 187 of SEQ ID NO:6 is itself a substrate of the protease,

Brown et al.('962) disclose processes of claims 45 and 66 that produce the product of claim 30 and also result in the cleavage of a substrate of claim 46 which is not a sterol-regulatory element-binding protein [SREBP]. Brown et al.('962) further anticipate claim 46 in disclosing, col. 17, lines 54-14, that the soluble, truncated SKI-1 variant lacking a transmembrane region and having an amino terminus at position 187 of SEQ ID NO:6 cleaves two artificial substrates that have peptide sequence of native substrates of SKI-1, one of which is not present in a SREBP and the other of which was a peptide substrate no longer within a SREBP.

Brown et al.('962) also anticipate limitations of claims 31-33 and 67-69 in disclosing, cols. 10 and 16 and Fig. 11A, that, following cleavage of the signal peptide region, the initial cleavage of the prodomain region results in a peptide, embraced by the terms "proteic" and "variant thereof" in claim 31, having an amino-terminus at about 18 and a carboxyl-terminus at position 137 which is secreted into the culture medium. This peptide has molecular weight of about 14kDa and is inherently capable of binding to an SKI-1 protease having, "in part" according to claim 31, the amino acid sequence from position 18 through position 1052, more specifically that part having the sequence from position 138 through position 1052 to which it was bound prior to cleavage and which, Brown et al.('962) at col. 16, line 33, is inhibitory to SKI-1 protease activity in association with the protease according to claim 33. The peptide is also a fragment of claim 32 and inherently capable of forming a "tight complex" with a soluble SKI-1 protease that lacks the transmembrane domain of SEQ ID NO:6 where it meets structural limitations of claim 31 not further limited by claim 32 and the functional limitations of claim 33 depending from claim 32. Because Brown et al.('962) disclose that the SKI-1 prodomain fragment is secreted into the medium, they also disclose compositions of claims 67-69.

Brown et al.('962) further disclose, at cols. 3-4, 66-71 and Figures 22 and 24, the

methods of claims 47-49, the peptides of claims 51-52, 54 and 55, notably the peptide set forth in SEQ ID NO:55 of Brown et al.('962), and the related methods of claims 59 and 60. This is because Brown et al.('962) disclose that they used a soluble SKI-1 produced recombinantly in cells transfected with a polynucleotide encoding a soluble SKI-1 protease conforming to limitations of clause (a) of claim 47 to cleave numerous peptide substrates, often flourogenically-labelled, often recovered for sequence determination, but not SREBPs, including the peptide set forth in their SEQ ID NO:55, which conforms to limitations of claims 51 and 52, which process is inherently a process of claims 59 and 60 because these claims neither require nor identify multiple candidate polypeptides used in methods for screening for SKI-1 activity or monitoring SKI-1 activity.

Claims 36, 40-44, 72, and 80-83 are anticipated by disclosures spanning cols. 4-5 of Brown et al.('962) of the preparation of expression constructs comprising an inducible promoter and a polynucleotide encoding a catalytically active SKI-1 and a transgenic cell comprising the expression constructs, as well as disclosures at the close of col. 5 and at cols. 22-33 of Brown et al.('962) of a polynucleotide encode a soluble, truncated, SKI-1, numerous recombinant, viral, expression vectors and host cells transformed therewith. Because claim 31 herein does not require that a soluble enzymatically active SKI-1 fragment be produced without a prodomain, indeed the specification discloses no such production of a soluble fragment unless it is expressed with the prodomain to ensure proper folding of the catalytic domain of this protease of the subtilase class of serine proteases, a polynucleotide of claim 36 is considered to encode a truncated SKI-1 capable of providing a soluble, truncated, SKI-1 having an amino-terminus at position 187 of SEQ ID NO:6 herein upon cleavage of the prodomain. Thus Brown et al.('962) inherently disclose the subject matters of claims 36, 40-44, 72, and 80-83 herein.

Allowable Subject Matter

Claims 53 and 56 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. It is also noted that Brown et al.('962) do not disclose a tight complex formed between any portion of the prodomain and the catalytic domain of a SKI-1 protease, which claim 32 herein falls short of describing, nor do they disclose Applicant's modifications of the prodomain amino acid sequence at pages 44-47 herein that support a modified prodomain having enhanced inhibitory capacity included within the scope of, but not specifically required by, claims 33-35 herein, nor disclose compositions comprising modified prodomain having enhanced inhibitory capacity included within the scope of, but not specifically required by, claim 33, thus comparable to those of claim 37 and 39 herein, nor a complex which claim 32 herein falls short of describing, nor a nucleic acid sequence encoding a modified prodomain having enhanced inhibitory capacity included within the scope of, but not specifically required by, claim 33, thus comparable to claim 39, or a composition comprising same of claim 75 herein.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at 703.308.3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct fax phone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
June 12, 2003